

REMARKS

This Response is to the final Office Action dated February 19, 2010 and the Advisory Action dated June 4, 2010. A Request for Continued Examination ("RCE") and a Petition for a one month extension of time is submitted herewith. The Commissioner is hereby authorized to charge \$810.00 for the RCE, \$490.00 for the Petition for a two month extension of time, and any additional fees that may be required or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 3712036-00746 on the account statement.

Claims 1-2, 4, 8-9, 11-16, 22-23 and 25 are pending in this application. Claims 5-7, 10, 24 and 26 were previously canceled without prejudice or disclaimer, and Claims 17-21 were previously withdrawn. In the Office Action, Claims 1-4, 9 and 15 are rejected under 35 U.S.C. §102. Claims 1-4, 8-9, 11-16, 22-23 and 25 are rejected under 35 U.S.C. §103. For at least the reasons set forth below, Applicants respectfully submit that the rejections should be reconsidered and withdrawn. Applicants note that the Patent Office has entered the amendments in the previous response filed May 5, 2010.

In the Office Action, Claims 1-4, 9 and 15 are rejected under 35 U.S.C. §102(b) as being anticipated by "*cis-trans* Lycopene Isomers, Carotenoids, and Retinol in the Human Prostate" to Clinton et al. ("*Clinton*"). In contrast, Applicants respectfully traverse the rejection for at least the reasons set forth below.

Applicants note that the Office Action cites *Clinton* in the initial anticipation rejection, but then refers to "HPLC Separation of Cis-Trans Carotene Isomers in Fresh and Processed Fruits and Vegetables" to Chandler et al ("*Chandler*") ("*Chandler*") for the main argument. In the previous response, Applicants presumed that the Patent Office meant to cite *Chandler* as the actual cited reference for the anticipation rejection instead of *Clinton* and responded accordingly. See, Amendment filed May 5, 2010. However, in the Advisory Action, the Patent Office states that "[t]he 102(b) anticipatory rejection is based on *Clinton* and that citation cor[r]esponds to the *Clinton* reference." See, Advisory Action, paragraph 11, lines 5-6. Applicants respectfully assert that the Patent Office still seems to be confused and improperly rejecting the present claims.

For example, the rejection under 35 U.S.C. §102(b) states that "*Chandler* et al. teaches provitamin A carotenoids are plentiful in human foods (Introduction, first paragraph). 38.8% cis

and 53% trans of canned tomato (Table 2, page 671). Thus, cis:trans at 30:70-90:10 is anticipated.” See, Final Office Action, page 2, lines 20-23. However, in the Advisory Action, the Patent Office explicitly states that “*Chandler*,” as mentioned in the first word of the above quotation, should read “*Clinton*.” This is not possible since *Clinton* does not disclose any of this information at any place at all in the disclosure. Instead, it is *Chandler* that discusses provitamin A carotenoids in the first paragraph of the introduction, and 38.8% cis and 53% trans of canned tomato in Table 2. Thus, Applicants submit that the anticipatory rejection from the Patent Office is both confusing and incorrect. Does the Patent Office intend to reject Claims 1-2, 4, 9 and 15 as anticipated in view of *Clinton* or *Chandler*? Applicants further submit that if it is, indeed, *Clinton* that the Patent Office meant to cite, the Patent Office should delete any reference to the *Chandler* reference, including the citations to the Introduction and Table 2, and provide proper support for the present claim limitations in the *Clinton* reference, which the Patent Office has currently failed to do.

Assuming that the Patent Office meant to cite *Clinton*, as is explicitly stated in the Advisory Action, Applicants submit that *Clinton* is deficient with respect to the present claims. Independent Claims 1, 9 and 15 recite, in part, a composition comprising at least one carotenoid-containing material, enriched in *cis*-isomer of the carotenoid compound, wherein the carotenoid-containing material is in a form selected from the group consisting of an extract, a concentrate, an oleoresin and combinations thereof. The carotenoid compound is selected from the group consisting of lycopene, zeaxanthine, beta-cryptoxanthin, capsanthine, canthaxanthine, phytofluene, phytoene, and combinations thereof, and the *cis:trans* isomer ratio of the carotenoid compound is from 30:70 to 90:10.

Carotenoids are natural products that have beneficial effects such as alleviating chronic diseases. Isolated or enriched carotenoid compounds extracted from a natural source such as a plant or an animal are already known in the art. However, the carotenoids in these naturally-occurring compounds are insufficiently bioavailable and, thus, their full beneficial effects cannot be realized. In contrast, the present claims provide a carotenoid compound with improved bioavailability. The *cis*-isomer content of naturally-occurring carotenoid compounds that are extracted from plants or animals is low. For this reason, after the naturally-occurring carotenoid compounds are extracted from the plant or animal, they are subjected to further treatment such as microwave irradiation or solubilisation followed by phase separation in order to modify the

isomer profile of the carotenoid. By subjecting the naturally-occurring carotenoid compound to additional treatment to increase its *cis*-isomer content such that the *cis:trans* isomer ratio is from 30:70 to 90:10, the bioavailability and/or bioefficacy of the carotenoid compound is increased.

In an embodiment, suitable plant or vegetable concentrates are obtainable by drying or freeze-drying the fresh-cut plants or vegetables or the respective roots, fruits or seeds thereof and then optionally grinding or granulating the dried material. Plant or vegetable extracts can be obtainable by extracting the fresh-cut or processed plants or vegetables or the respective roots, fruits or seeds thereof for example with water or with one or more food grade solvents or with a mixture of water and one or more food grade solvents. Preferably, the extracts and concentrates according to the present claims may be lipidic or aqueous. Because carotenoids are liposoluble, extraction with water will remove unwanted constituents that are water-soluble such as sugars, amino acids, soluble proteins, organic acids, for example.

In another embodiment, the carotenoid-containing material is an oleoresin. For example, oleoresins are obtained by lipidic extraction using a solvent compatible with the food business, cosmetics or pharmaceuticals. Oleoresins prepared by conventional methods have a content in carotenoid of about 0.05% to 50% by weight. Their content of all-trans isomer of carotenoids is usually higher than that of *cis* isomers, e.g. the ratio of *cis-trans* isomers of lycopene in a selected tomato oleoresin is about 7:93. Oleoresins are preferred starting material for obtaining the primary composition according to the present invention, because they contain other carotenoids or antioxidants such as Vitamin E, which also stabilize the composition. The activity and stability of the carotenoid compound in the oleoresin is improved, in particular during the isomerisation process and the yield of the *cis*-lycopene in the primary composition is also increased.

The carotenoid-containing material that is in the form of an extract, a concentrate or an oleoresin can be subjected to a microwave irradiation or to other treatments including non-thermal treatments. Conditions of the microwave irradiation depend on the quantity and quality of the material. If an oleoresin is used, the power and time are adjusted so that the temperature of the microwave oven is of at least 100 °C, preferably from 100 to 180 °C and most preferably from 115 to 140 °C. If an aqueous extract is used, a medium adapted to microwave irradiation may be used. The aim of the medium is to solubilize or disperse carotenoids. The losses can be minimised when the isomerisation is performed under nitrogen in the presence of antioxidants

and in the absence of light. The isomerisation yield may also be improved by adding exogenous lipids in the medium.

The isomers of carotenoid-containing compound generated thereof may be subjected to a further treatment intended to modify the isomer profile of the primary composition according to the intended use. The enrichment in some specific *cis*-isomers can be achieved by solubilisation of *cis*-isomers in selected organic solvents followed by phase separation using centrifugation or filtration, for example. The *cis:trans* isomer ratio in the final primary composition can then be 30:70 to 90:10.

Clinton fails to disclose or suggest a composition comprising at least one carotenoid-containing material, enriched in *cis*-isomer of the carotenoid compound, wherein the *cis:trans* isomer ratio of the carotenoid compound is from 30:70 to 90:10, and wherein the carotenoid-containing material is in a form selected from the group consisting of an extract, a concentrate, an oleoresin and combinations thereof as required, in part, by independent Claims 1, 9 and 15. Instead, *Clinton* discloses that the *trans*-lycopene in tomatoes, tomato paste and tomato soup accounts for 79 to 91% of the total lycopene. Similarly, the *cis*-lycopene in tomatoes, tomato paste and tomato soup accounts for 9 to 21% of the total lycopene. See, *Clinton*, Abstract, right column. While *Clinton* may teach higher ratios of *cis/trans*-isomers of lycopene in serum or prostate tissues, these tissues are not considered food compositions or stable products for consumption. Indeed, serum or prostate tissues are not fit for ingestion in oral compositions or for use in cosmetic compositions, nor would these bodily elements be considered useful for same. Further, serum and/or prostate tissues are not carotenoid-containing material in a form selected from the group consisting of an extract, a concentrate, an oleoresin and combinations thereof as required, in part, by independent Claims 1, 9 and 15.

The problem of stability with higher *cis/trans* ratios is not insignificant since the problem with lycopene is that it is naturally in its stable all-*trans* form instead of *cis*. Because *Clinton* is entirely aimed at quantifying serum and tissues levels of lycopene and fails to disclose or suggest a composition comprising at least one carotenoid-containing material, enriched in *cis*-isomer of the carotenoid compound, wherein the *cis:trans* isomer ratio of the carotenoid compound is from 30:70 to 90:10, and wherein the carotenoid-containing material is in a form selected from the group consisting of an extract, a concentrate, an oleoresin and combinations thereof, as required,

in part, by independent Claims 1, 9 and 15, *Clinton* fails to anticipate the currently amended claims.

Further, anticipation is a factual determination that “requires the presence in a single prior art disclosure of each and every element of a claimed invention.” *Lewmar Marine, Inc. v. Barient, Inc.*, 827 F.2d 744, 747 (Fed. Cir. 1987) (emphasis added). Federal Circuit decisions have repeatedly emphasized the notion that anticipation cannot be found where less than all elements of a claimed invention are set forth in a reference. See, e.g., *Transclean Corp. v. Bridgewood Services, Inc.*, 290 F.3d 1364, 1370 (Fed. Cir. 2002). As such, a reference must clearly disclose each and every limitation of the claimed invention before anticipation may be found. For at least these reasons, Applicants respectfully submit that *Clinton* fails to anticipate the presently claimed subject matter.

Further, assuming that the Patent Office meant to cite *Chandler* for the anticipation rejection, which Applicants do not believe is the case, *Chandler* fails to disclose or suggest a number of elements of the present claims. *Chandler* fails to disclose or suggest a carotenoid-containing material in a form selected from the group consisting of an extract, a concentrate, an oleoresin and combinations thereof and having a *cis:trans* isomer ratio from 30:70 to 90:10 of a carotenoid compound as required by independent Claims 1, 9 and 15. *Chandler* also fails to disclose or suggest a carotenoid-containing material having a *cis:trans* isomer ratio from 30:70 to 90:10 of a carotenoid compound selected from the group consisting of lycopene, zeaxanthine, beta-cryptoxanthin, capsanthine, canthaxanthine, phytofluene, phytoene, and combinations thereof as required by independent Claims 1, 9 and 15.

The Patent Office asserts that *Chandler* discloses a canned tomato as being an extracted and concentrated tomato. Applicants respectfully submit that a canned tomato disclosed by *Chandler* is merely that, one or more tomatoes in a can. The tomato may be processed in the form of being cooked or sterilized, but there is no evidence in *Chandler* that the canned tomato includes any tomato in the form of an extract, a concentrate or an oleoresin.

Chandler further discloses separation and identification of *cis*- and *trans*- isomers of alpha- and beta-carotene. See *Chandler*, Title (“HPLC Separation of *Cis-Trans* Carotene Isomers in Fresh and Processed Fruits and Vegetables”); Introduction, page 669, paragraphs 3-5. Furthermore, the tables relied on by the Patent Office merely show the percentage of *cis*- and *trans*-isomers of beta-carotene. See *Chandler*, Tables 1-2. Nowhere does *Chandler* disclose or

suggest a carotenoid compound selected from the group consisting of lycopene, xeaxanthine, beta-cryptoxanthin, capsanthine, canthaxanthine, phytofluene, phytoene, and combinations thereof in which the *cis:trans* isomer ratio is from 30:70 to 90:10.

For at least the reasons discussed above, Applicants respectfully submit that independent Claims 1, 9 and 15, along with any of the claims that depend from Claims 1, 9 and 15, are novel, nonobvious and distinguishable from both *Clinton* and *Chandler*.

Accordingly, Applicants respectfully request that the rejection of the pending claims under 35 U.S.C. §102 be reconsidered and withdrawn.

In the Office Action, Claims 1-2, 4, 8-9, 11-16, 22-23 and 25 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,965,183 to Hartal et al. ("*Hartal*") in view of "HPLC Separation of Cis-Trans Carotene Isomers in Fresh and Processed Fruits and Vegetables" to Chandler et al ("*Chandler*"). Applicants respectfully traverse the rejection for at least the reasons set forth below.

Hartal and *Chandler* alone or in combination fail to disclose or suggest each and every element of the present claims. In addition, the skilled artisan would have no reason to combine *Hartal* and *Chandler* to arrive at the claimed invention.

Hartal and *Chandler* alone or in combination also fail to disclose or suggest a carotenoid-containing material having a *cis:trans* isomer ratio from 30:70 to 90:10 of a carotenoid compound selected from the group consisting of lycopene, xeaxanthine, beta-cryptoxanthin, capsanthine, canthaxanthine, phytofluene, phytoene, and combinations thereof as required by independent Claims 1, 9, 15 and 22. *Hartal* and *Chandler* alone or in combination fail to disclose or suggest a carotenoid-containing material in a form selected from the group consisting of an extract, a concentrate, an oleoresin and combinations thereof and having a *cis:trans* isomer ratio from 30:70 to 90:10 of a carotenoid compound as required by independent Claims 1, 9, 15 and 22. *Chandler* is deficient with respect to the present claims as previously discussed.

Hartal discloses providing stable lycopene compositions with a high staining power for use in food coloring. See *Hartal*, column 2, lines 17-40. Nowhere does *Hartal* disclose or suggest any carotenoid-containing material having a *cis:trans* isomer ratio from 30:70 to 90:10 of a carotenoid compound in a form such as a lipidic extract or an oleoresin or even enriching the *cis*-isomer content of the lycopene to increase its bioavailability. In fact, the Patent Office

admits that *Hartal* fails to disclose any *cis:trans* isomer ratio of from 30:70 to 90:10 and the specific carotenoid compounds. See, Final Office Action, page 1, lines 1-22.

The Patent Office nevertheless asserts that merely because lycopene is a type of carotenoid, one of ordinary skill in the art would reasonably expect that lycopene could be used as the type of carotenoid taught by *Chandler*. However, *Chandler* specifically states that the column used in its experiments “is highly selective toward carotene isomers and under the solvent conditions employed other carotene[oids] such as lycopene do not elute.” See *Chandler*, page 671, paragraph 2, lines 13-15. As such, one of ordinary skill in the art would not consider lycopene an obvious modification of carotene and would have no reason to use lycopene in the column of *Chandler* to analyze *cis-trans* isomer content.

Moreover, one of ordinary skill in the art understands that lycopene is distinct from carotene because *cis*-isomers of carotenoids only exist naturally for beta-carotene, not for lycopene. *Chandler* discloses that certain fresh fruits such as plums and nectarines have a *cis*-isomer content of beta-carotene greater than 20%. See *Chandler*, Table 2. In contrast, the *cis*-isomer content of lycopene for a tomato oleoresin is merely 7%. In order to increase the *cis*-isomer content of lycopene to greater than 20%, the oleoresin must be subjected to further treatment such as microwave irradiation or solubilisation followed by phase separation. Therefore, the *cis*-isomer content of carotene disclosed in *Chandler* is not necessarily the same for lycopene or any other carotenoid and, contrary to the Patent Office’s assertion, cannot be relied on for the disclosure of a *cis:trans* isomer ratio from 30:70 to 90:10 in the claimed carotenoid compounds.

Furthermore, one of ordinary skill in the art would have no reason to combine the cited references because *Chandler* teaches away from the present claims. In this regard, references must be considered as a whole and those portions teaching against or away from each other and/or the claimed invention must be considered. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve Inc.*, 796 F.2d 443 (Fed. Cir. 1986). “A prior art reference may be considered to teach away when a person of ordinary skill, upon reading the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the Applicant.” *Monarch Knitting Machinery Corp. v. Fukuhara Industrial Trading Co., Ltd.*, 139 F.3d 1009 (Fed. Cir. 1998), quoting, *In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994).

Chandler is entirely directed to determining the amount of *cis*- and *trans*- isomers of beta-carotene in certain food products to assess the vitamin A activity of the food products. See *Chandler*, page 669, Introduction, paragraphs 2-3 and 5. *Chandler* specifically teaches that “[i]somerization reactions of the all *trans* form to *cis*-isomers reduces the bioavailability of the carotenoids as vitamin A precursors.” See *Chandler*, page 669, paragraph 2, lines 4-6. *Chandler* further notes that the conversion of *trans* beta-carotene isomers to *cis*-isomers results in a 15 – 35 % loss of vitamin A value. See *Chandler*, page 669, paragraph 3, lines 2-5. Therefore, *Chandler* teaches away from increasing the *cis:trans* isomer content of a carotenoid to increase its bioavailability.

In contrast, the present claims are entirely directed to a compound enriched in *cis*-isomer of the carotenoid compound. In order to obtain a carotenoid compound with an increased *cis*-isomer content, a naturally occurring extract or oleoresin of carotenoid is subjected to further treatment intended to modify its isomer profile. By increasing the *cis:trans* isomer ratio up to from 30:70 to 90:10, the present claims provide a carotenoid compound with a higher bioavailability than the compound alone. This is in direct contrast to *Chandler*’s teaching that a higher *cis*-isomer content reduces the bioavailability of the carotenoid. Therefore, *Chandler* teaches away from compounds enriched in *cis*-isomer of the carotenoid compound in accordance with the present claims.

For at least the reasons discussed above, Applicants respectfully submit that independent Claims 1, 9, 15 and 22, along with any of the claims that depend from Claims 1, 9, 15 and 22, are novel, nonobvious and distinguishable from *Hartel* and *Chandler*.

Accordingly, Applicants respectfully request that the rejection of the pending claims under 35 U.S.C. §103(a) be reconsidered and withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims that could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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